Fig. 1

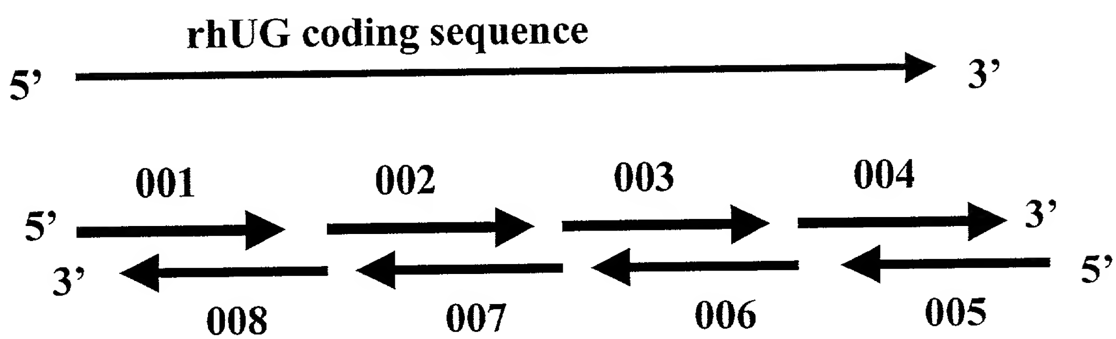


Fig. 2

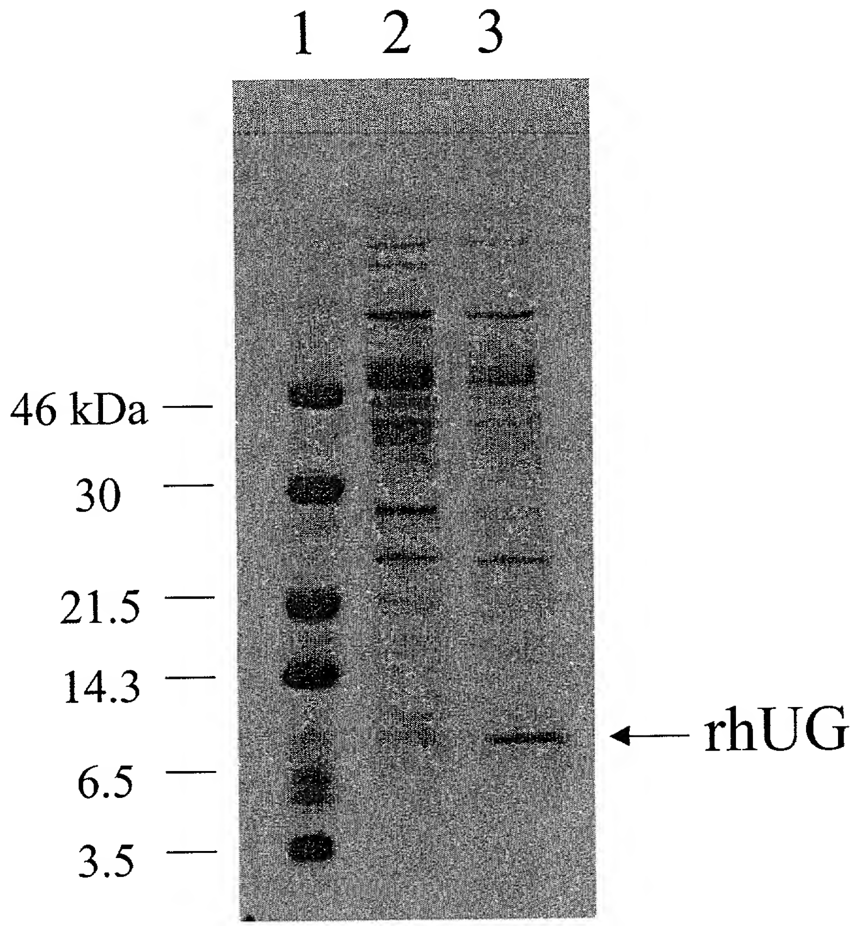


Fig. 3

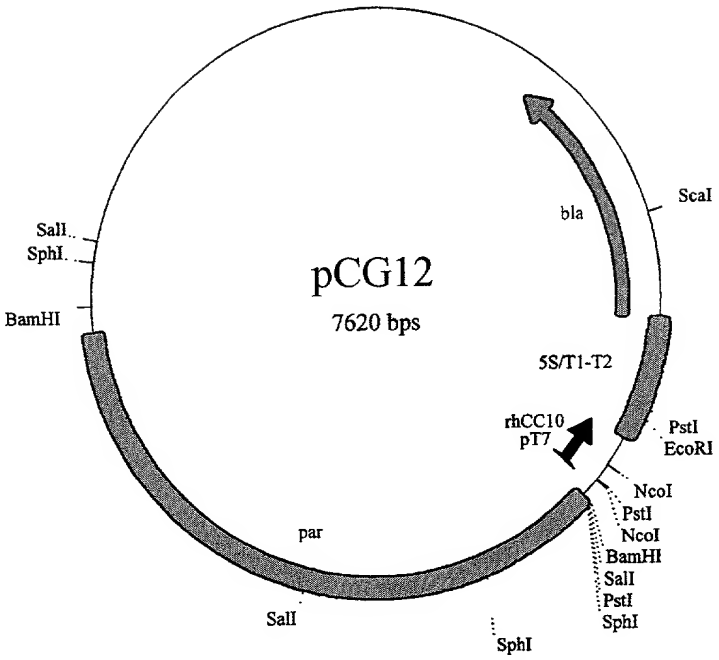


Fig. 4

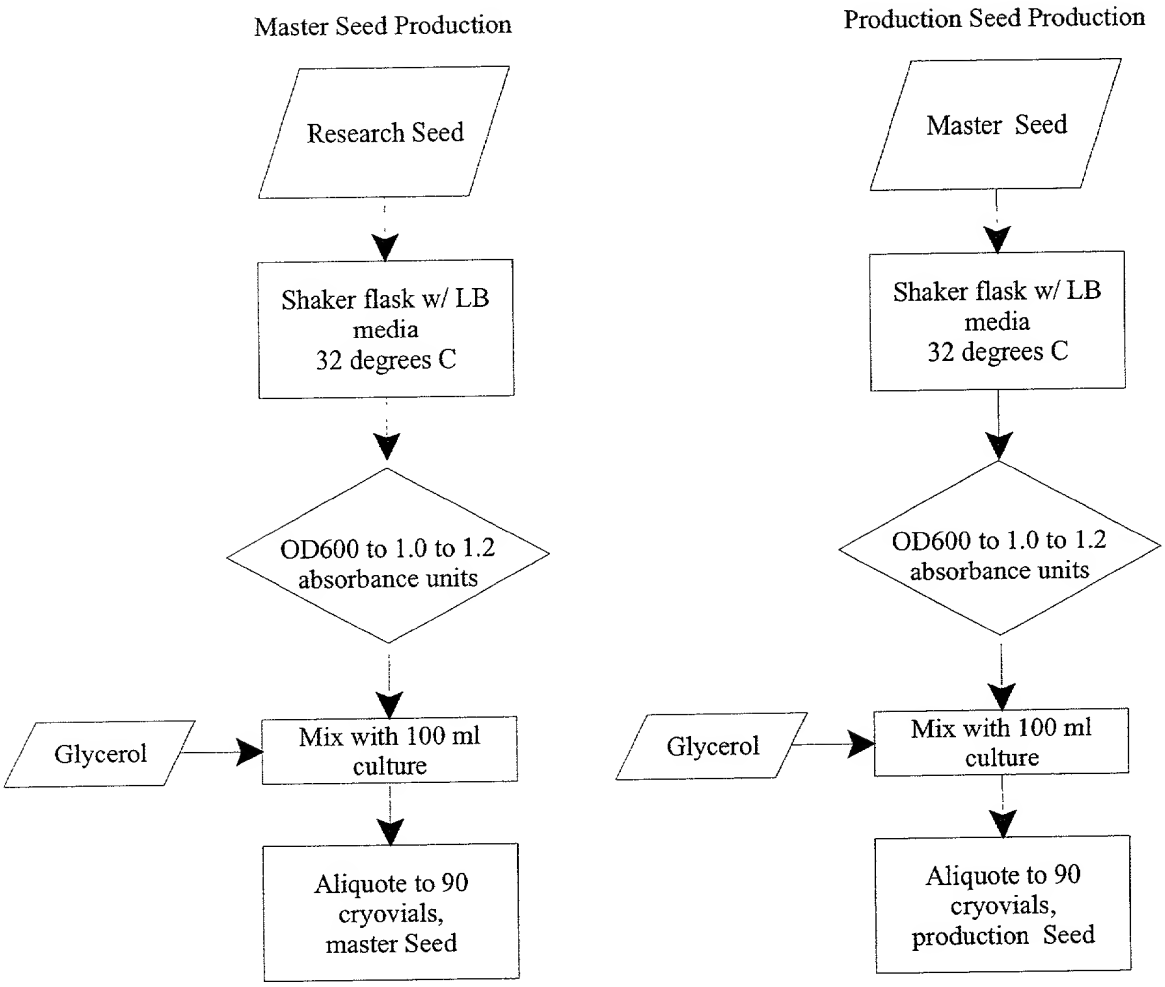


Fig. 5

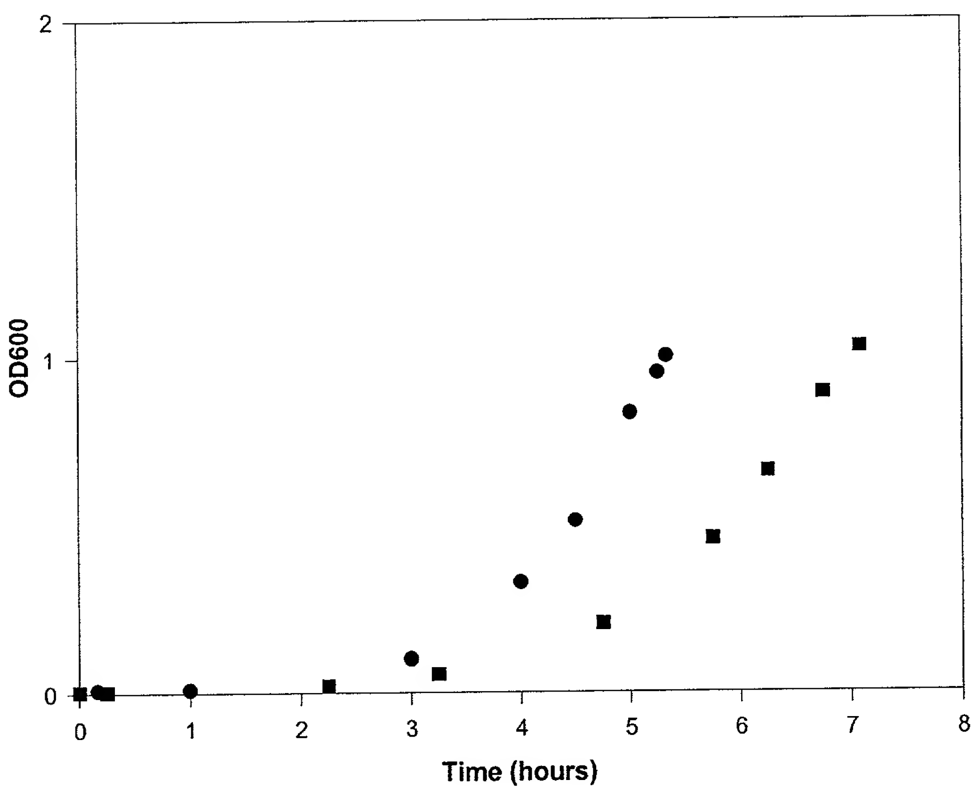
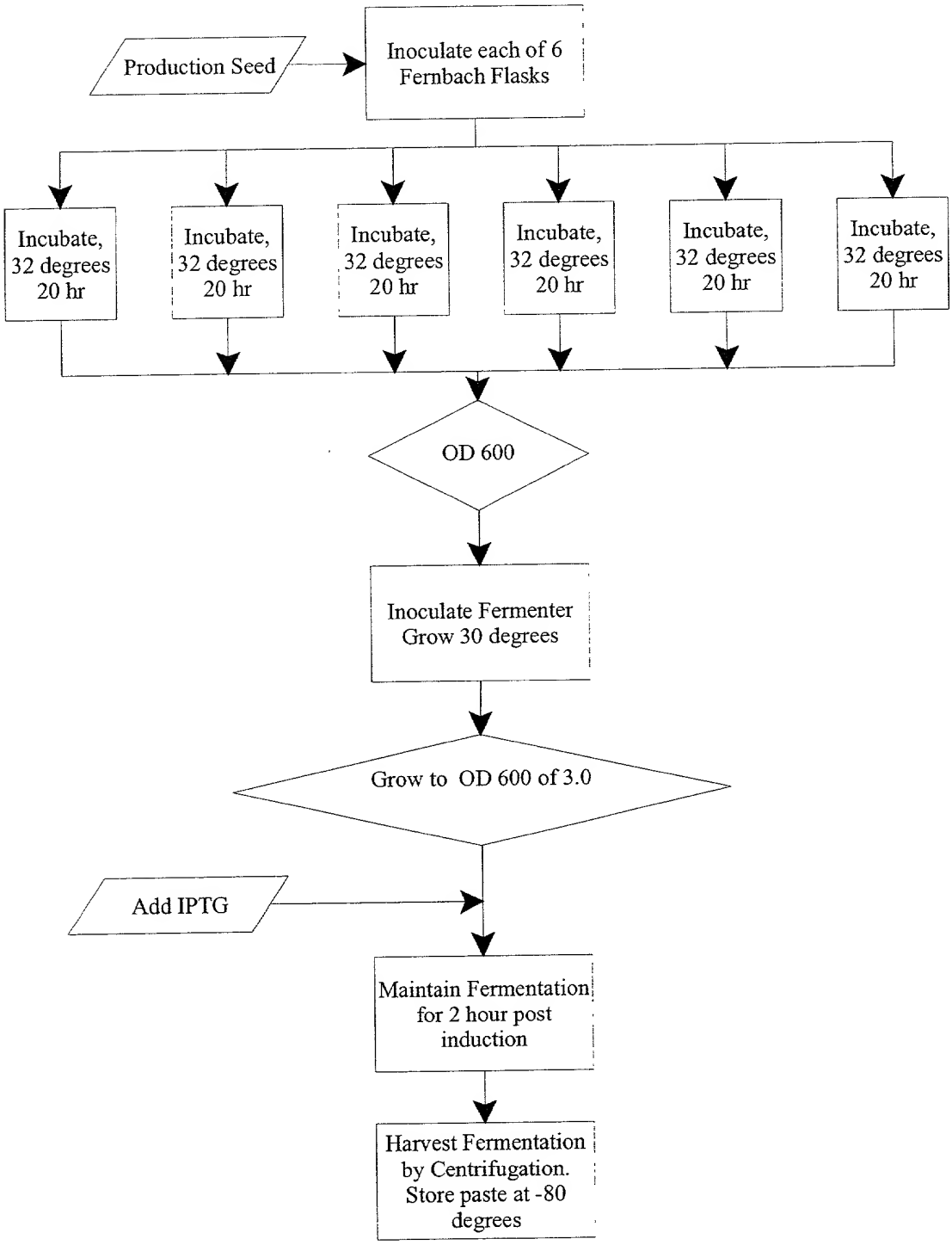


Fig. 6



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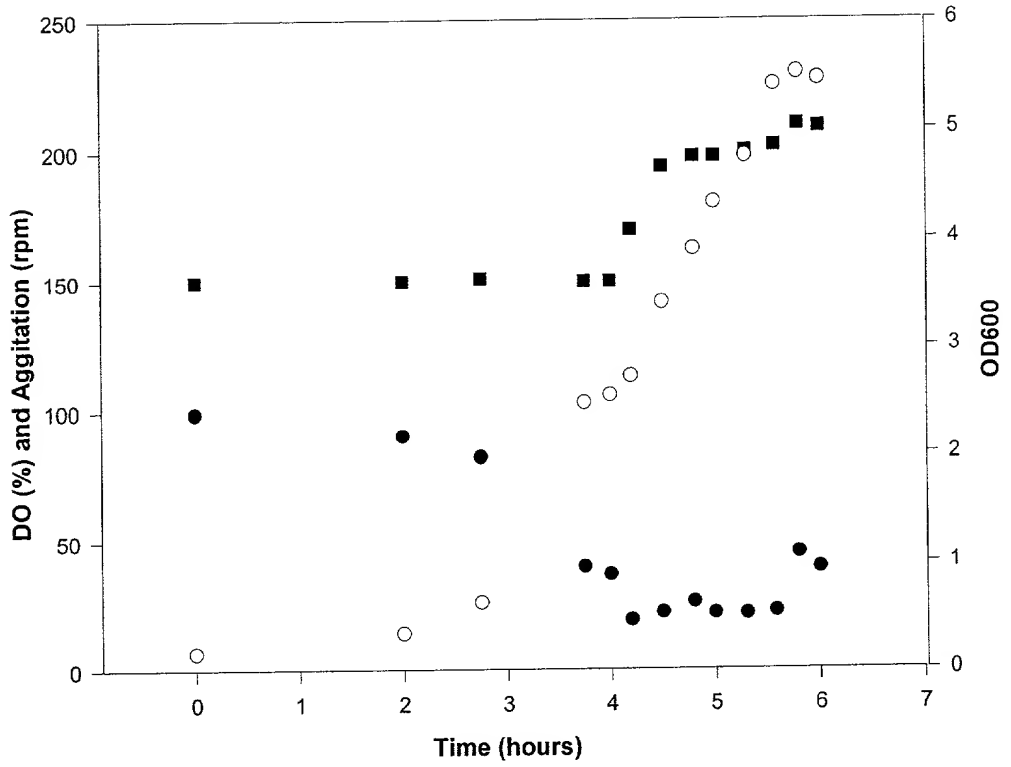

Fig. 8

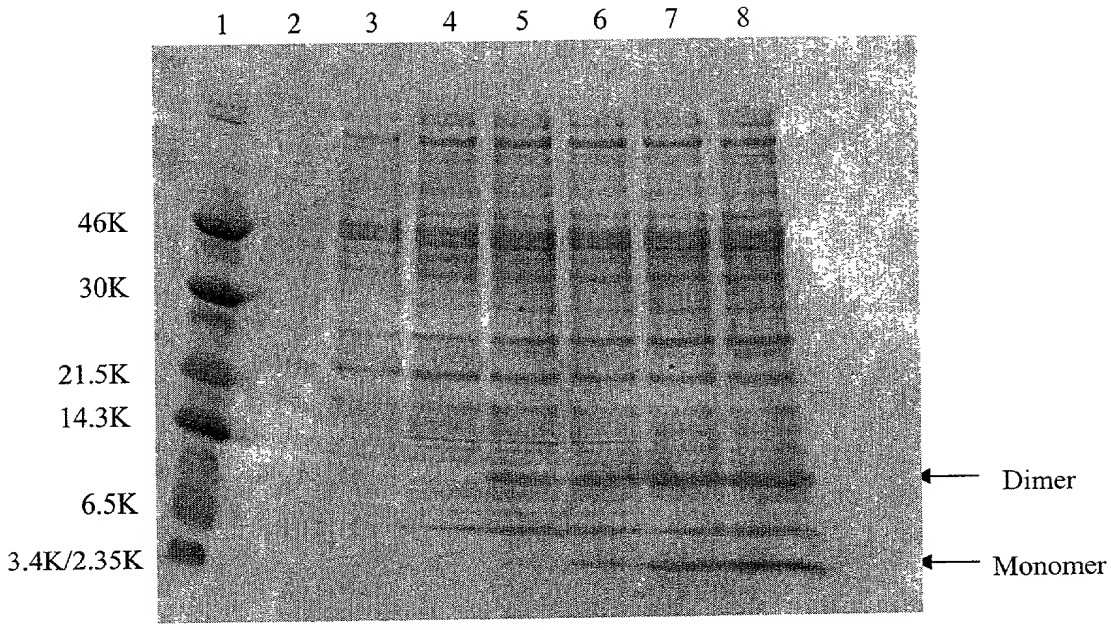

Fig. 9a

Purification used in Initial Toxicology study

Cell Lysis by Shear

↓

Tangential Flow Filtration, Polyethersulfone Membrane (100,000 NMWCO)

↓

Tangential Flow Filtration, Concentration Polyethersulfone Membrane (5,000 NMWCO)

↓

Anion Exchange Chromatography, Elution with Sodium Chloride

↓

Tangential Flow Filtration, Concentration/Buffer exchange Polyethersulfone Membrane (5,000 NMWCO)

↓

Type I, Hydroxyapatite, Elution with Sodium Phosphate

↓

Tangential Flow Filtration, Polyethersulfone Membrane (30,000 NMWCO)

↓

Tangential Flow Filtration, Concentration/Buffer Exchange Polyethersulfone Membrane (5,000 NMWCO)

Fig. 9b

Purification used in first cGMP Manufacturing Run

Cell Lysis by Shear

↓

Tangential Flow Filtration, Polyethersulfone Membrane (100,000 NMWCO)

↓

Tangential Flow Filtration, Concentration /Diafiltration Polyethersulfone Membrane (5,000 NMWCO)

↓

Anion Exchange Chromatography, Elution with Sodium Chloride

↓

Tangential Flow Filtration, Concentration/Buffer exchange Polyethersulfone Membrane (5,000 NMWCO)

↓

Type I, Hydroxyapatite, Elution with Sodium Phosphate

↓

Copper Immobilized Metal Affinity Chromatography

↓

Filtration through SartoBind Q Anion Exchange Membrane

↓

Tangential Flow Filtration, Concentration/Buffer Exchange Polyethersulfone Membrane (5,000 NMWCO)

Fig. 10

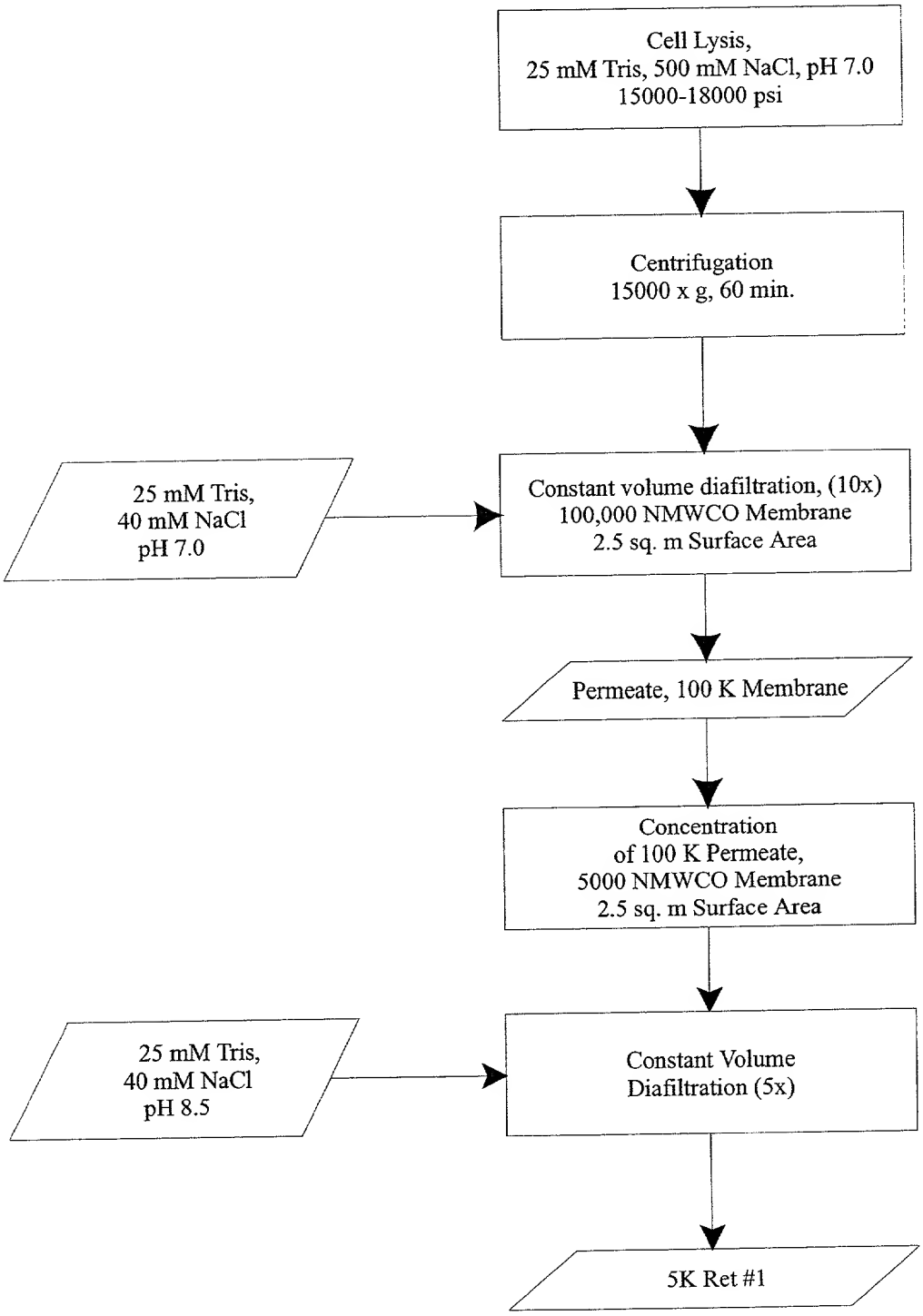

Fig. 11a

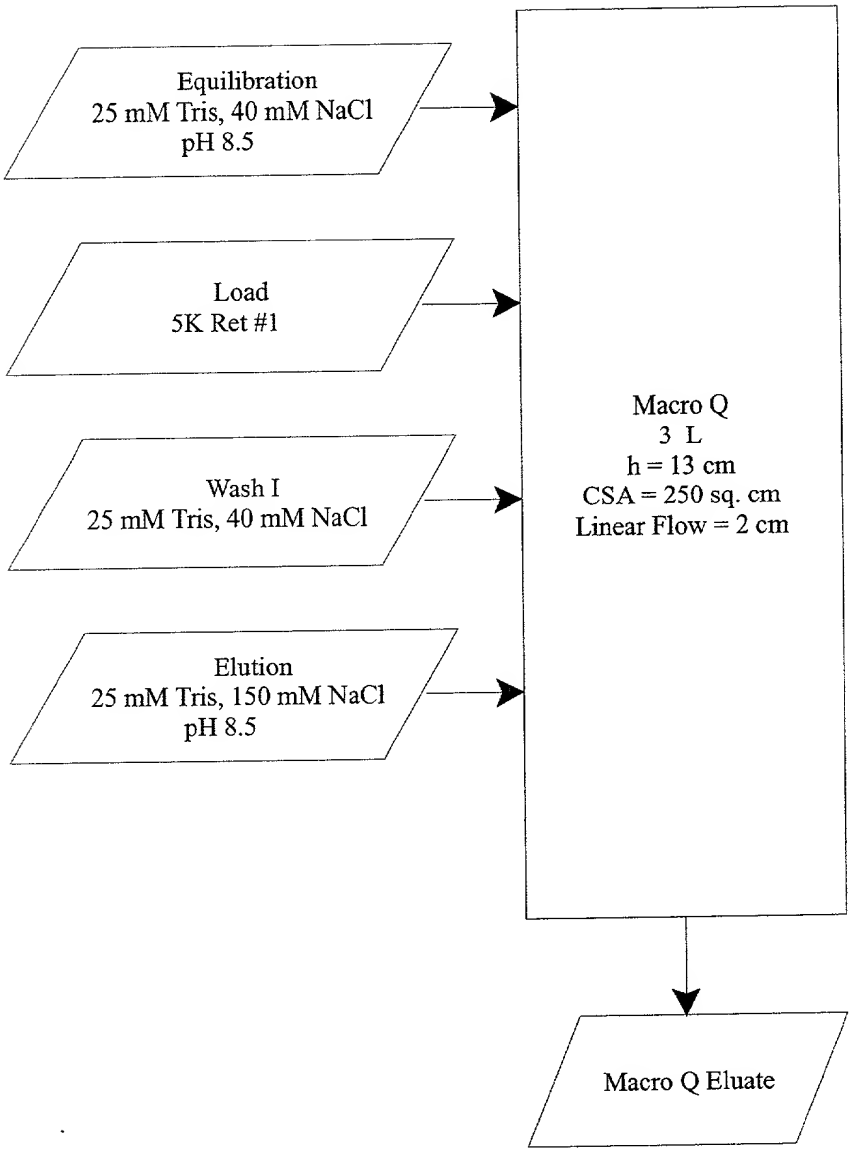

Fig. 11b

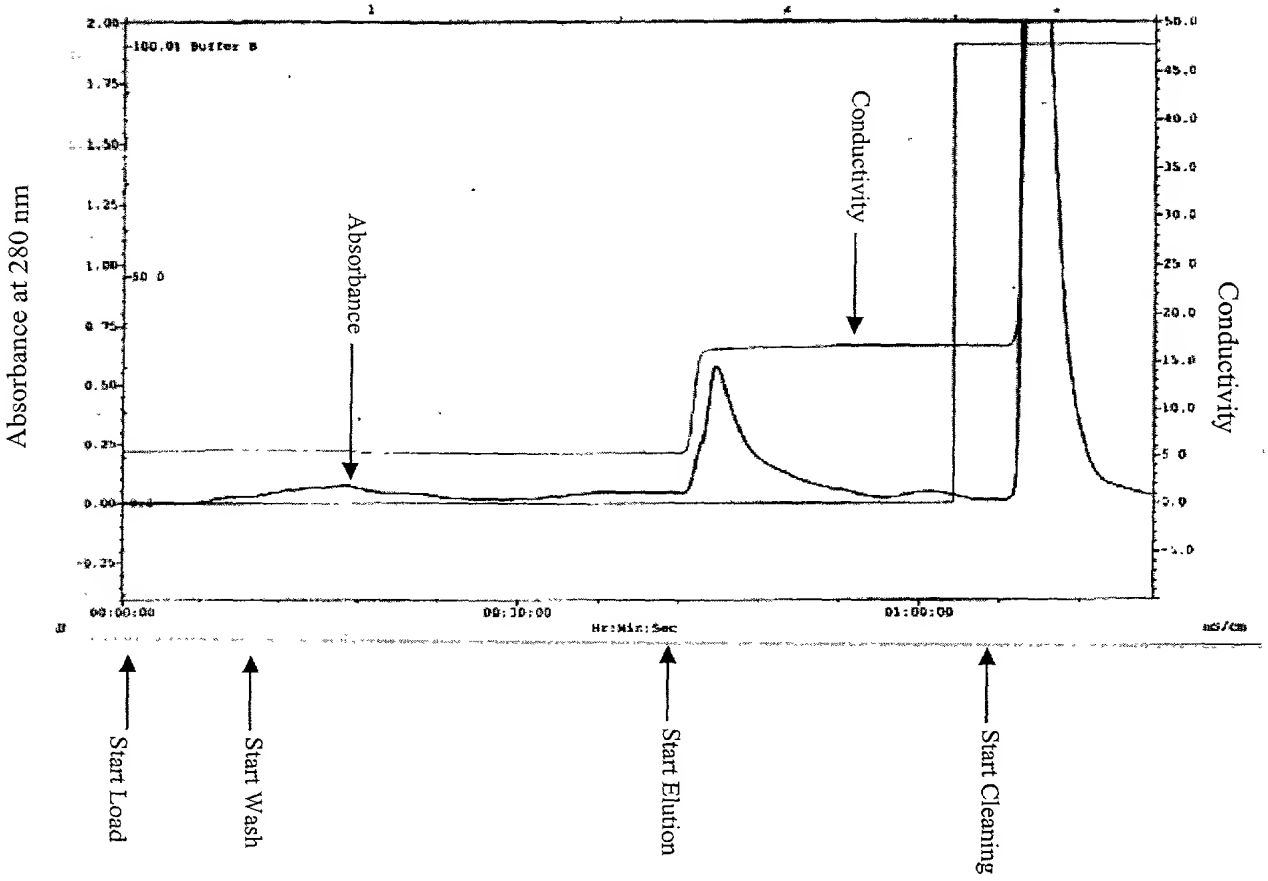
Absorbance at 280 nm
Absorbance
Conductivity
Conductivity
Start Load
Start Wash
Start Elution
Start Cleaning

Fig. 12

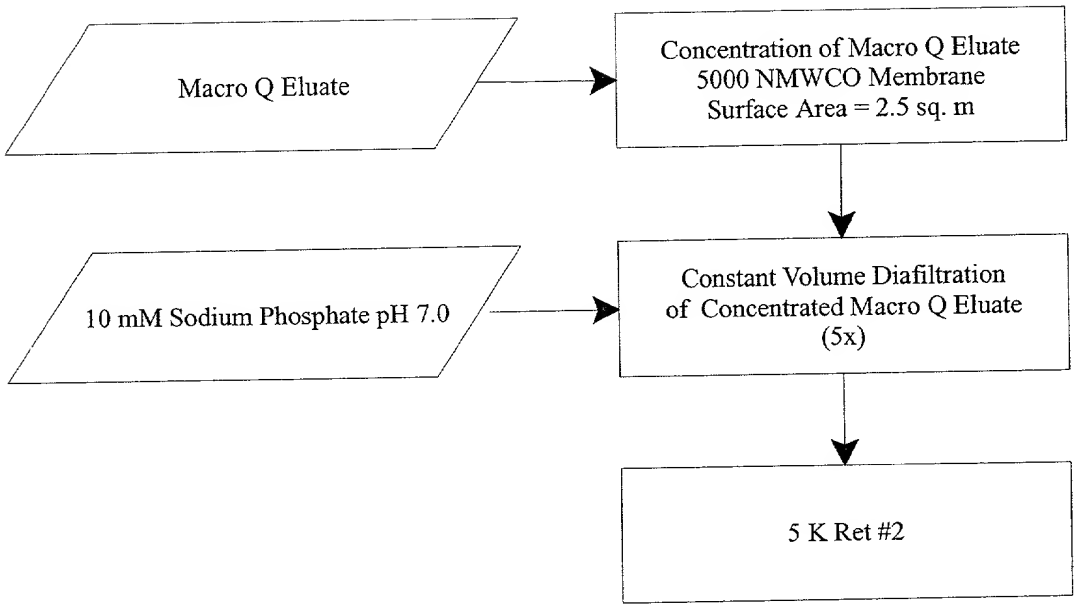

Fig. 13a

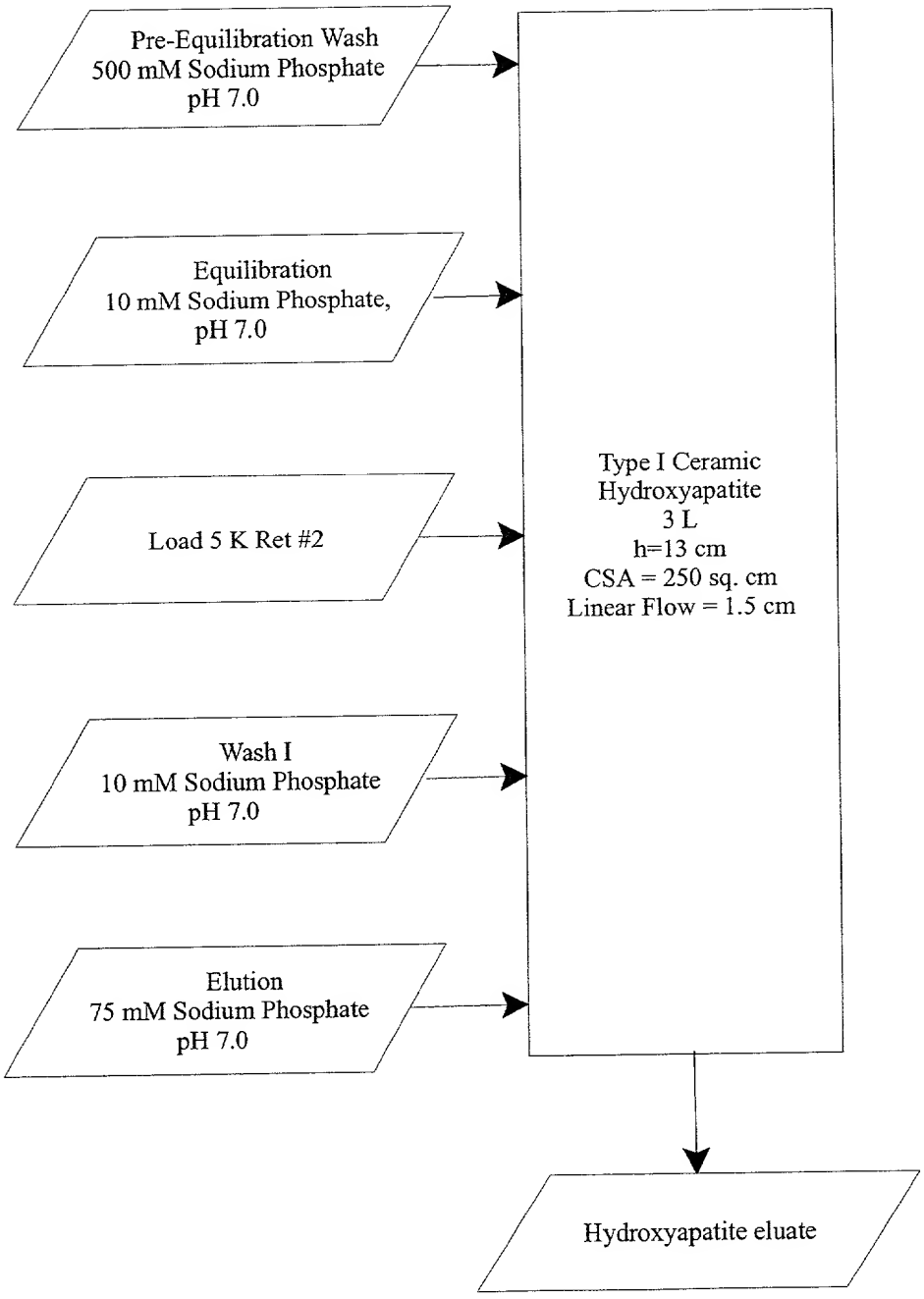

Fig. 13b

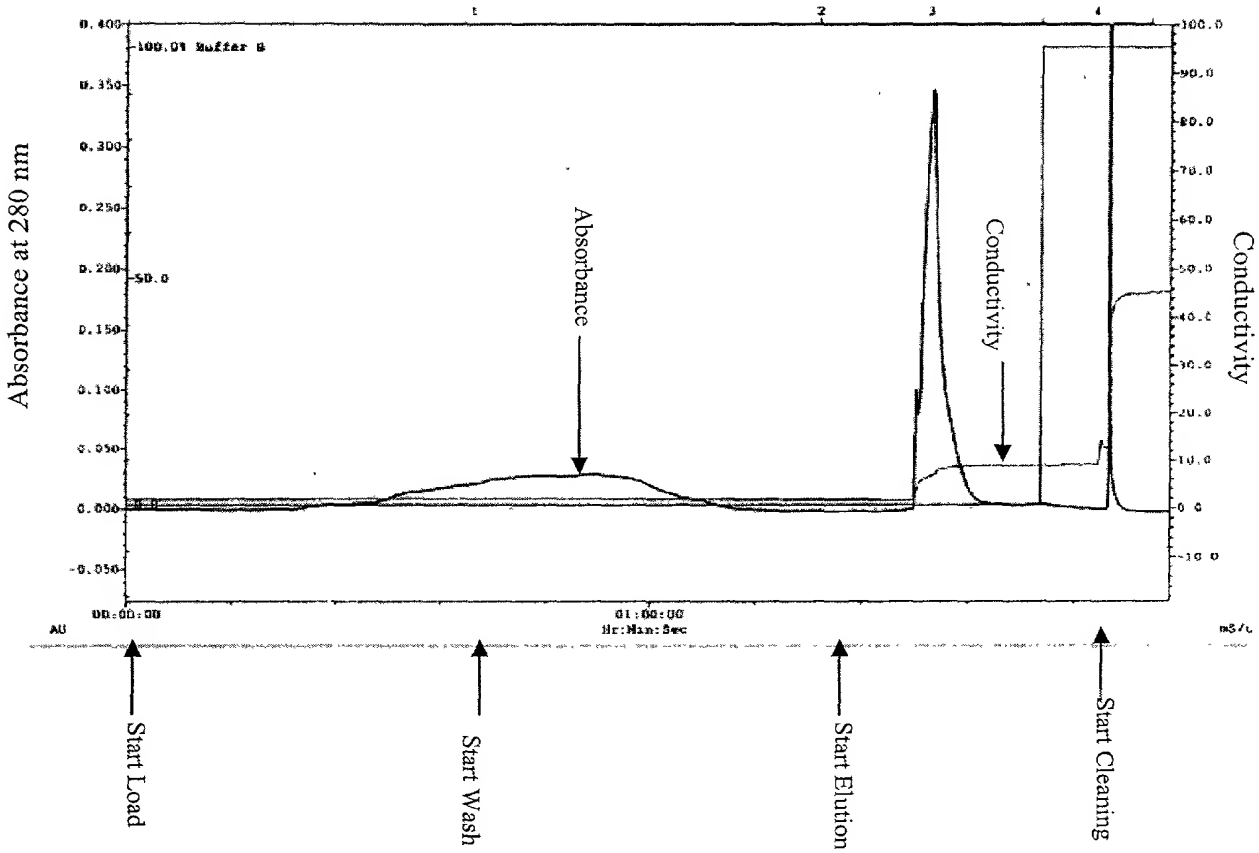
Absorbance at 280 nm
Absorbance
Conductivity
Conductivity
Start Load
Start Wash
Start Elution
Start Cleaning

Fig. 14a

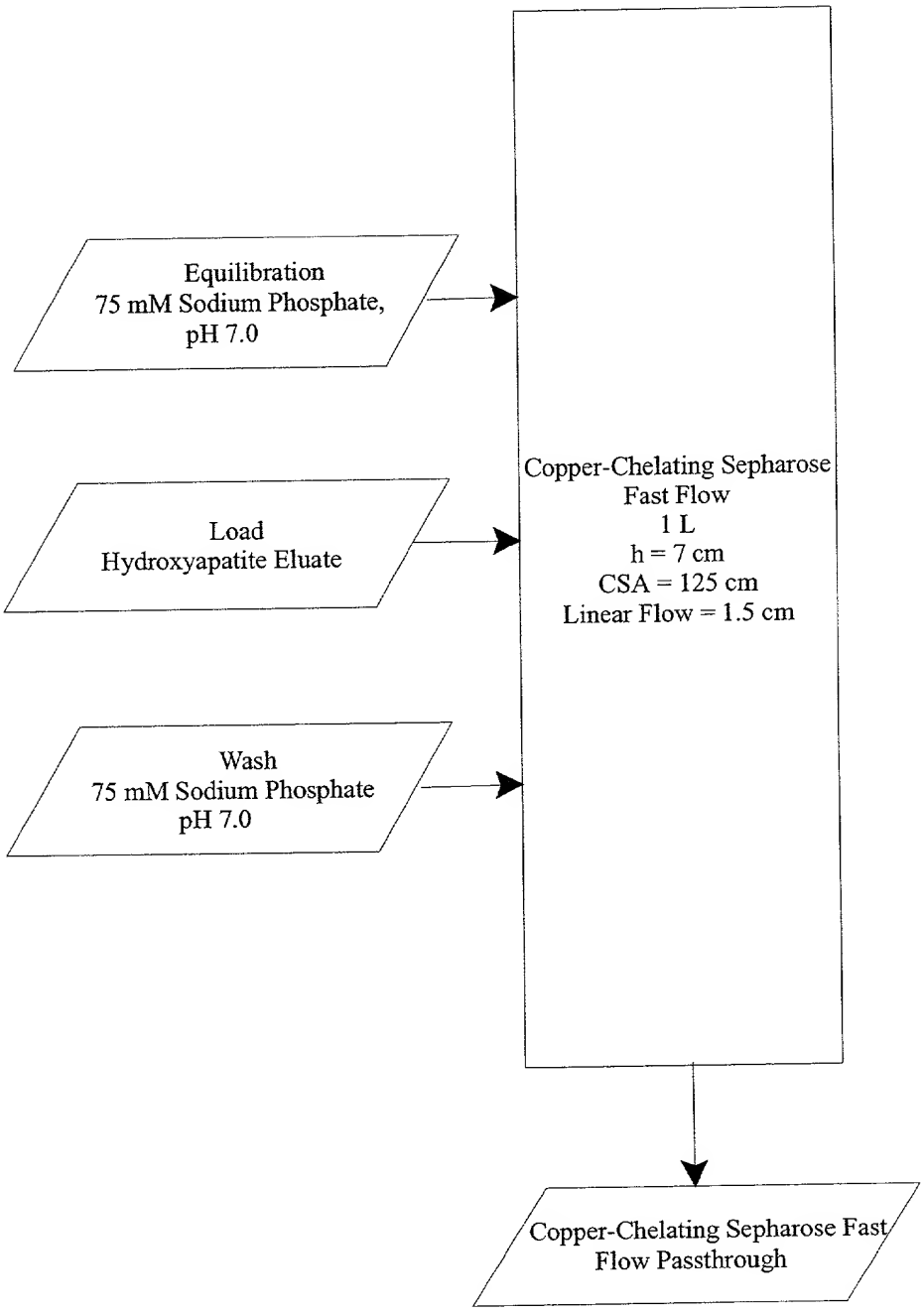
Equilibration
75 mM Sodium Phosphate,
pH 7.0
Load
Hydroxyapatite Eluate
Wash
75 mM Sodium Phosphate
pH 7.0
Copper-Chelating Sepharose
Fast Flow
1 L
h = 7 cm
CSA = 125 cm
Linear Flow = 1.5 cm
Copper-Chelating Sepharose Fast
Flow Passthrough

Fig. 14b

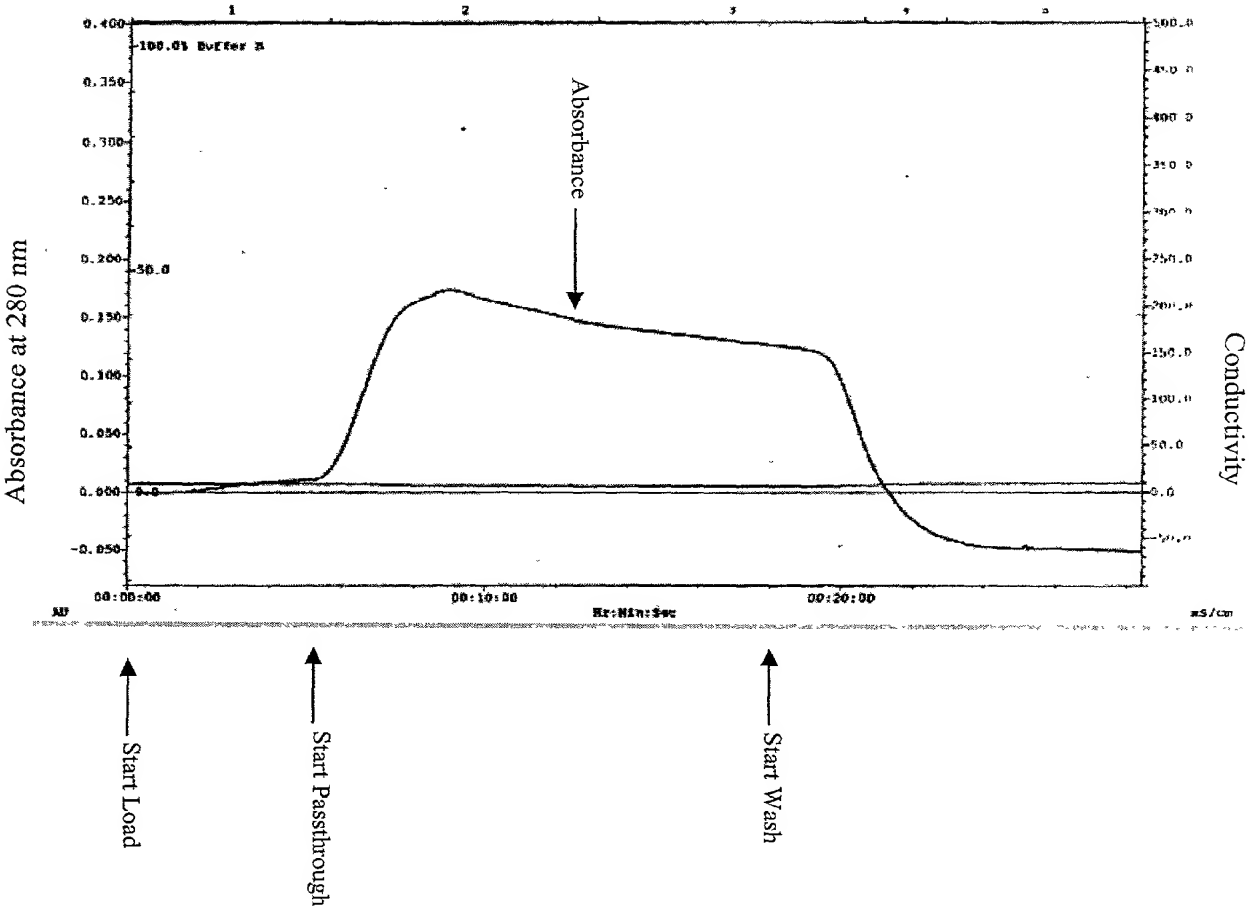
Absorbance at 280 nm
Absorbance
Conductivity
Start Load
Start Passthrough
Start Wash

Fig. 15

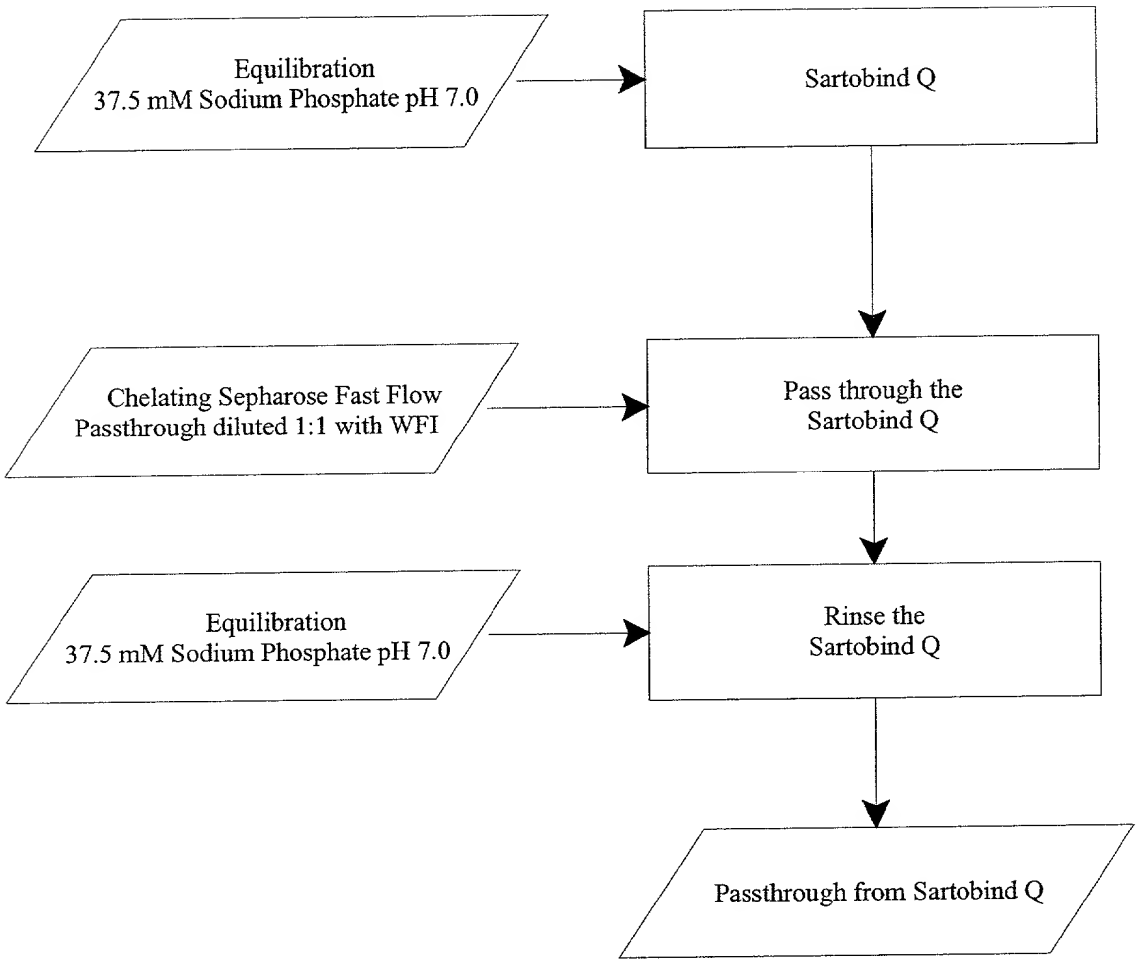

Fig. 16

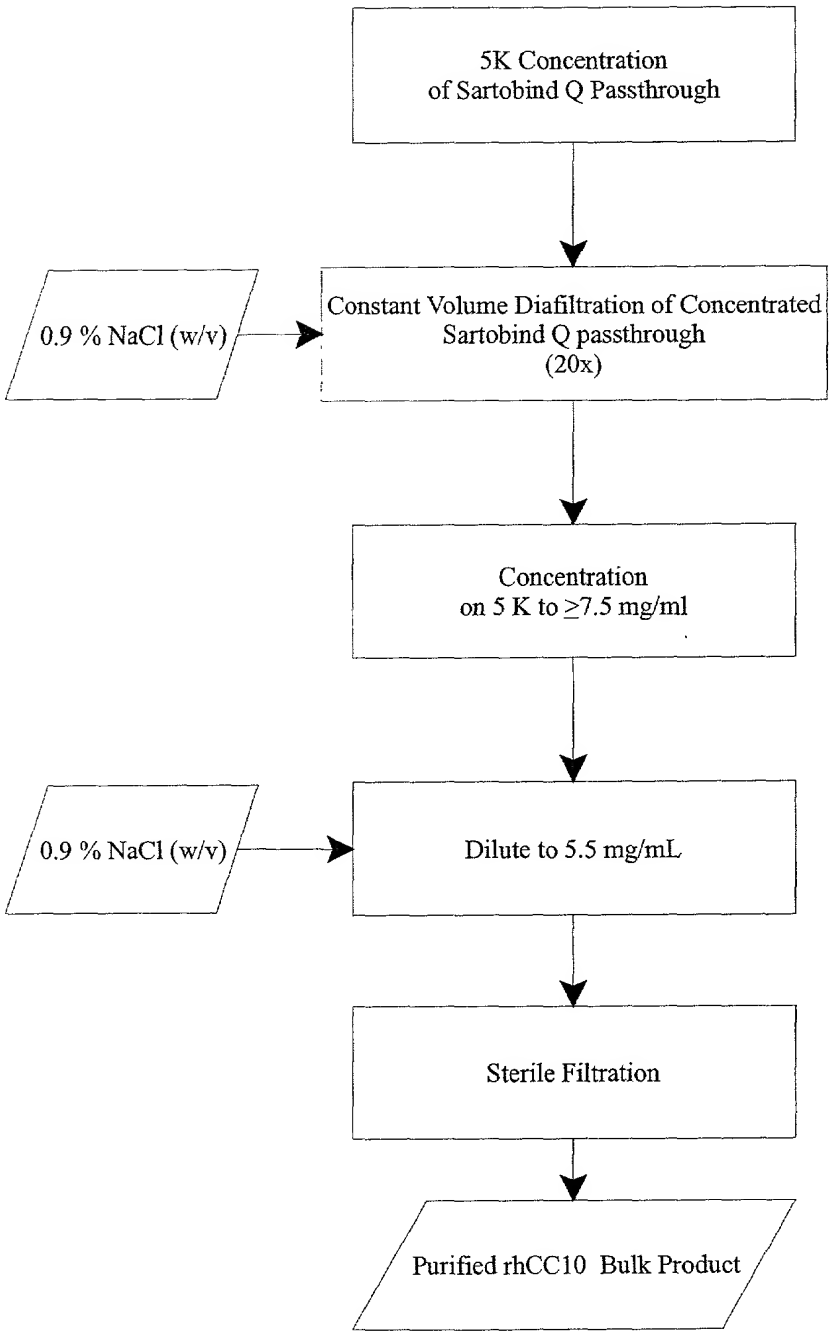

Fig. 17

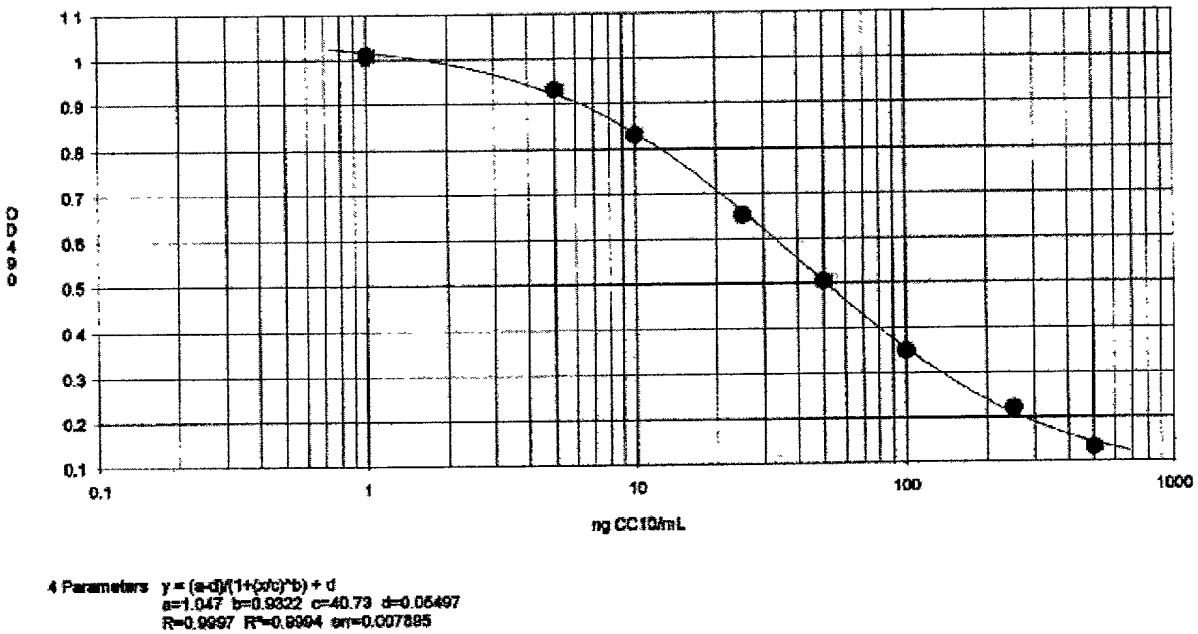

Fig. 18

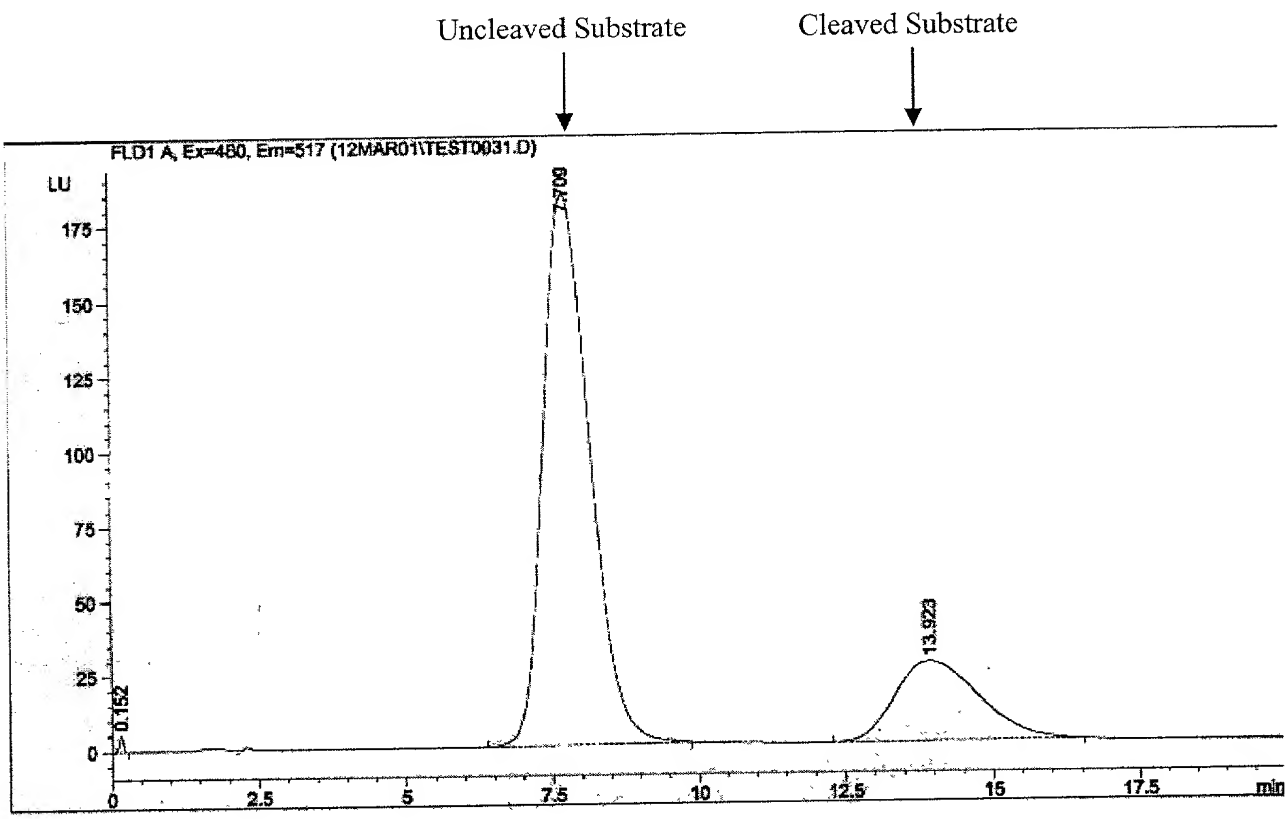

Fig. 19

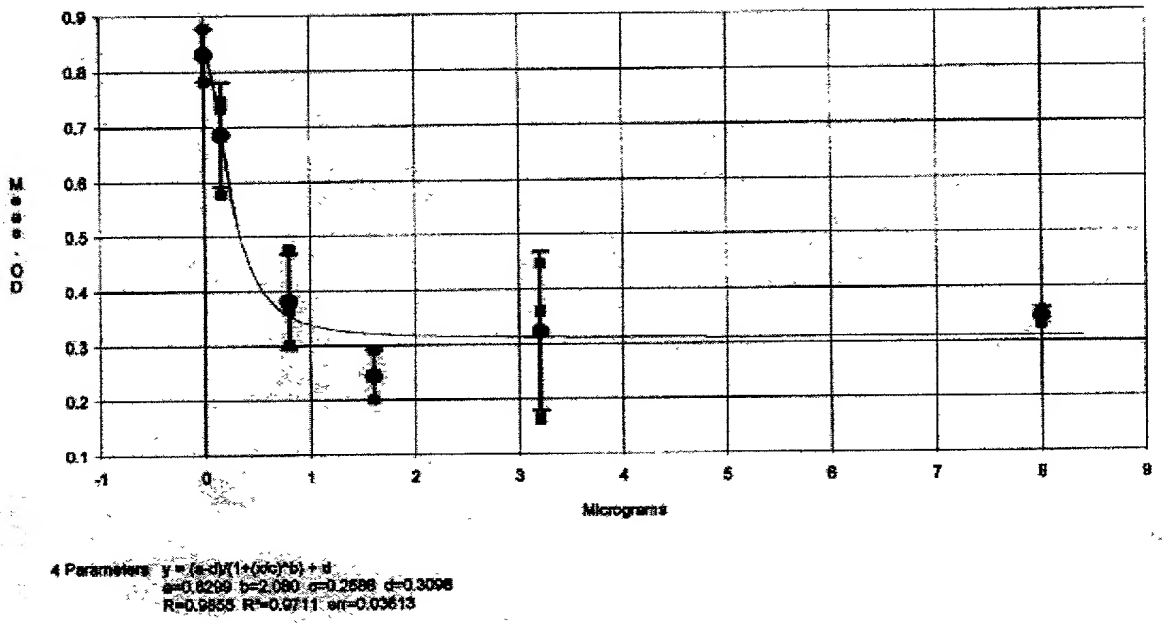

Fig. 20a

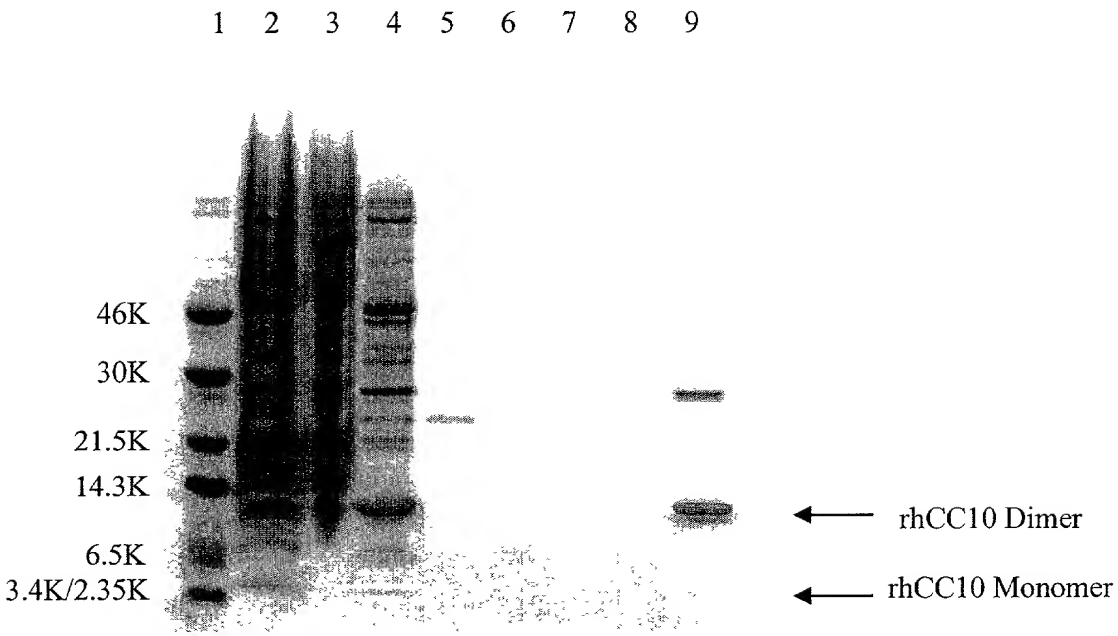

Fig. 20b

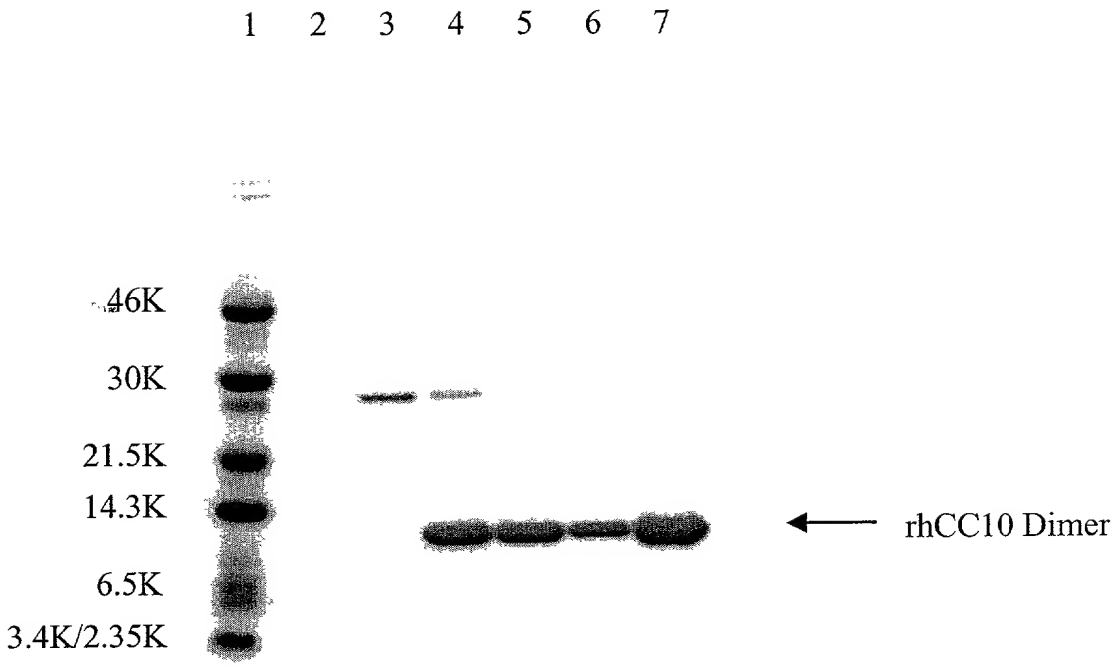

Fig. 21

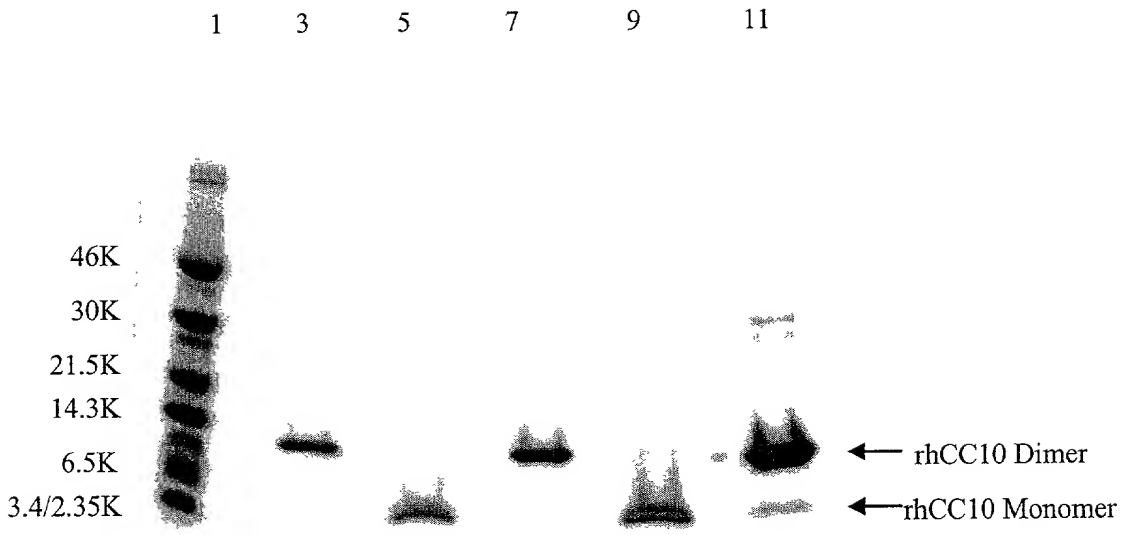

Fig. 22

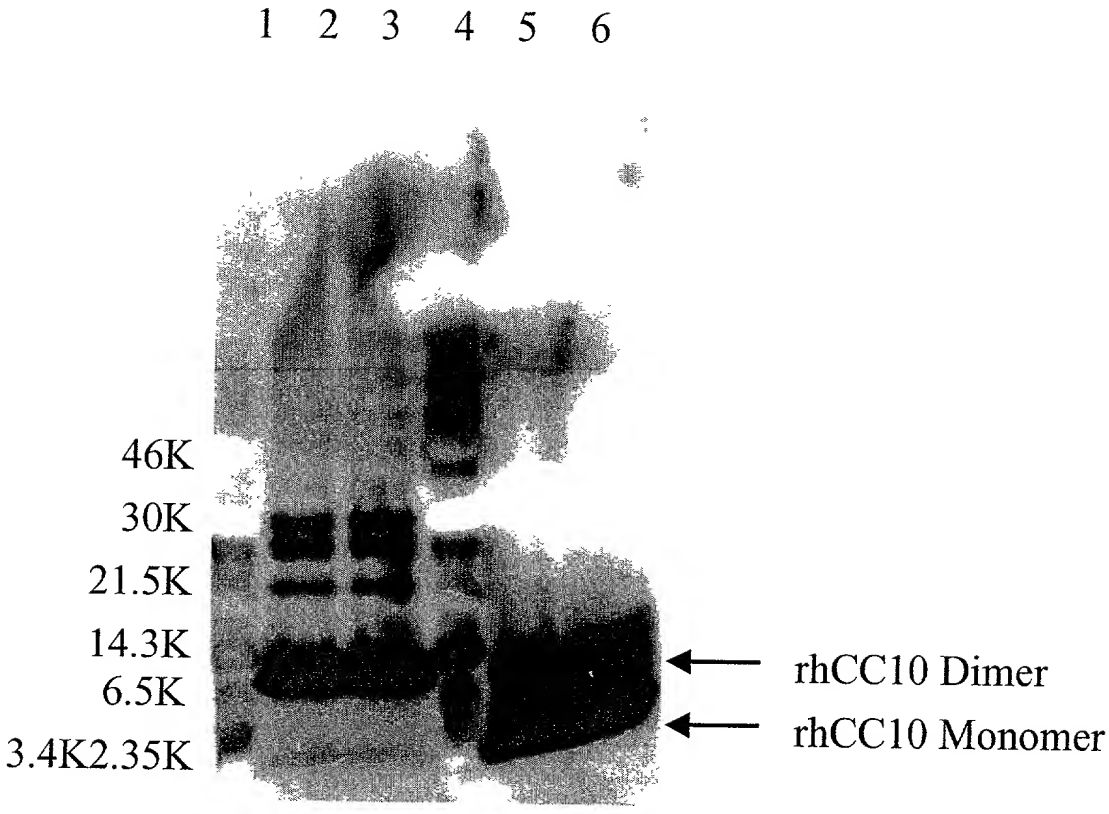

Fig. 23

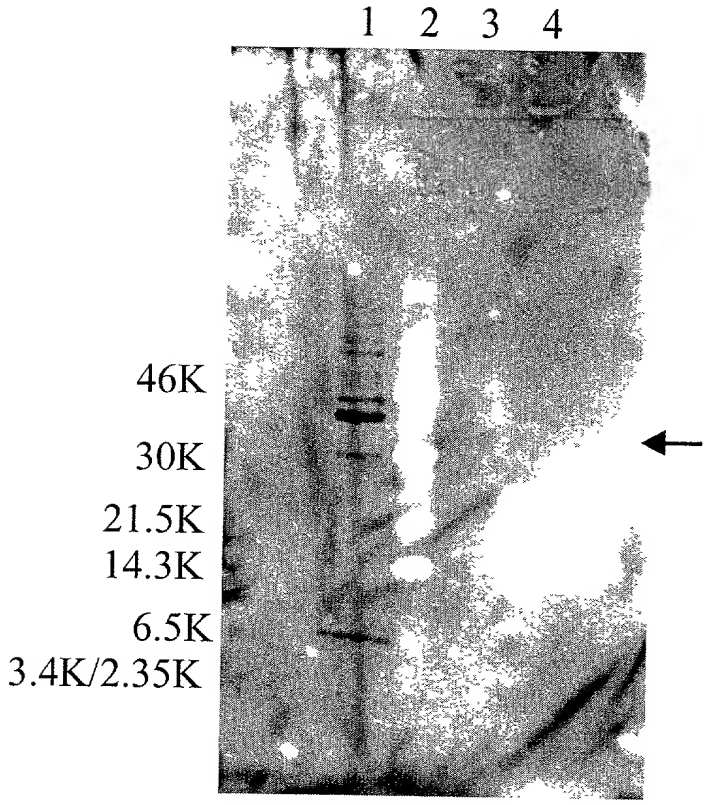

Fig. 24

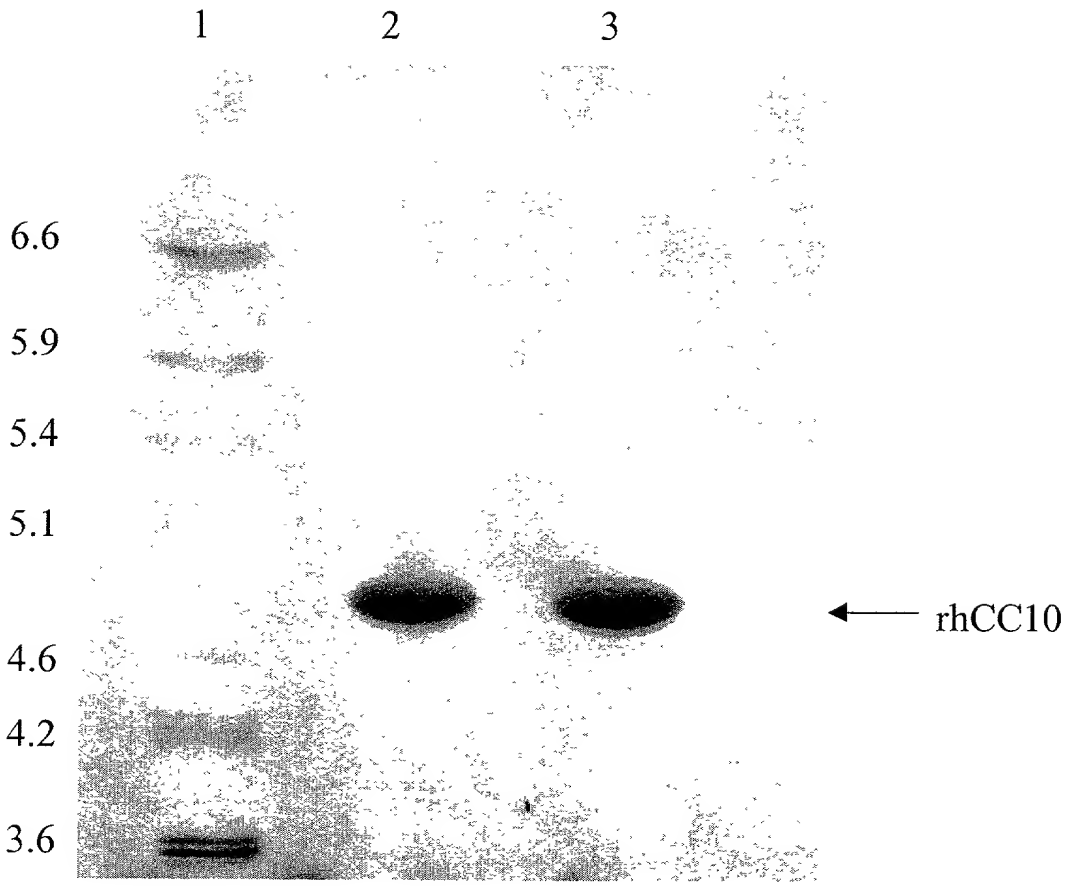

Fig. 25

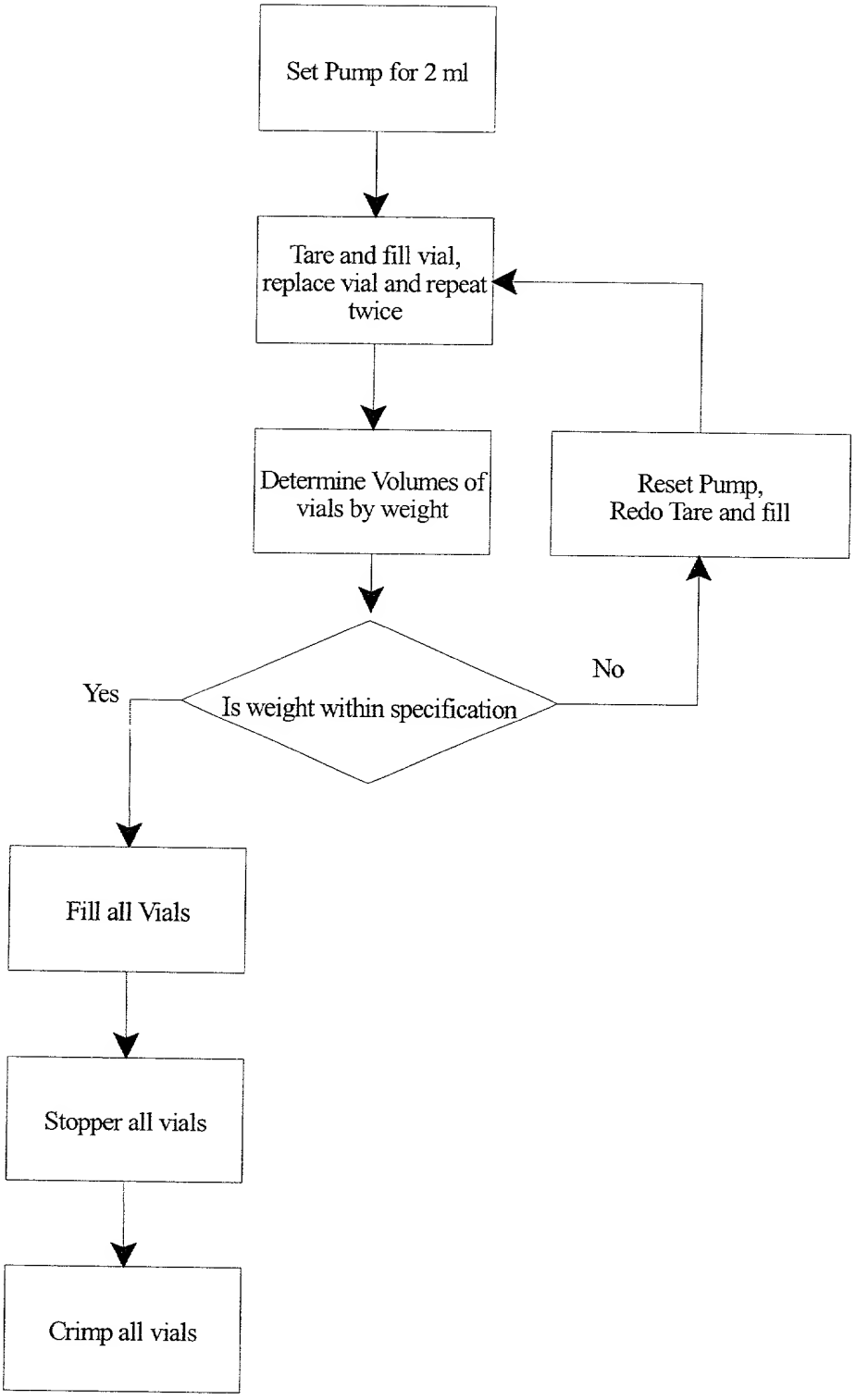

Fig. 26

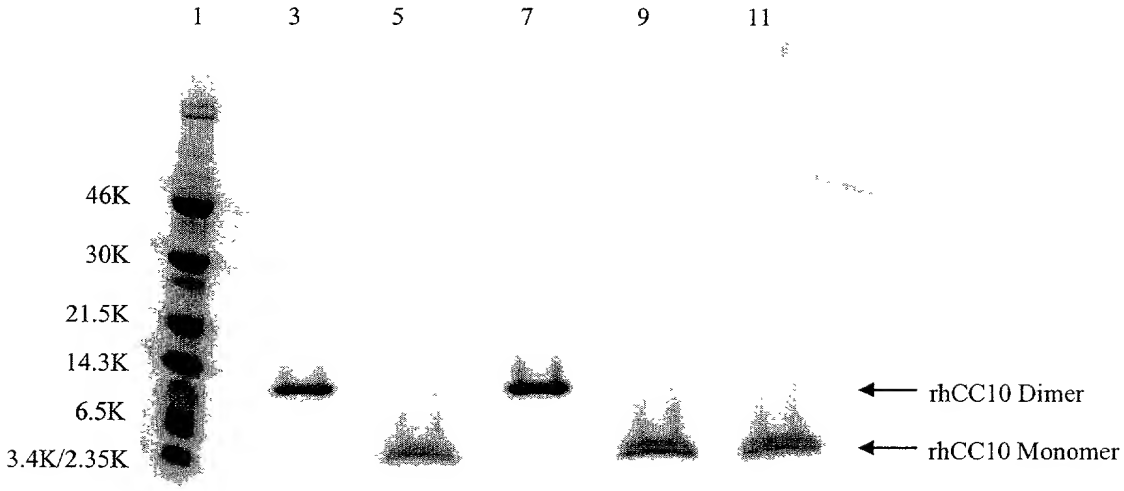

Fig. 27

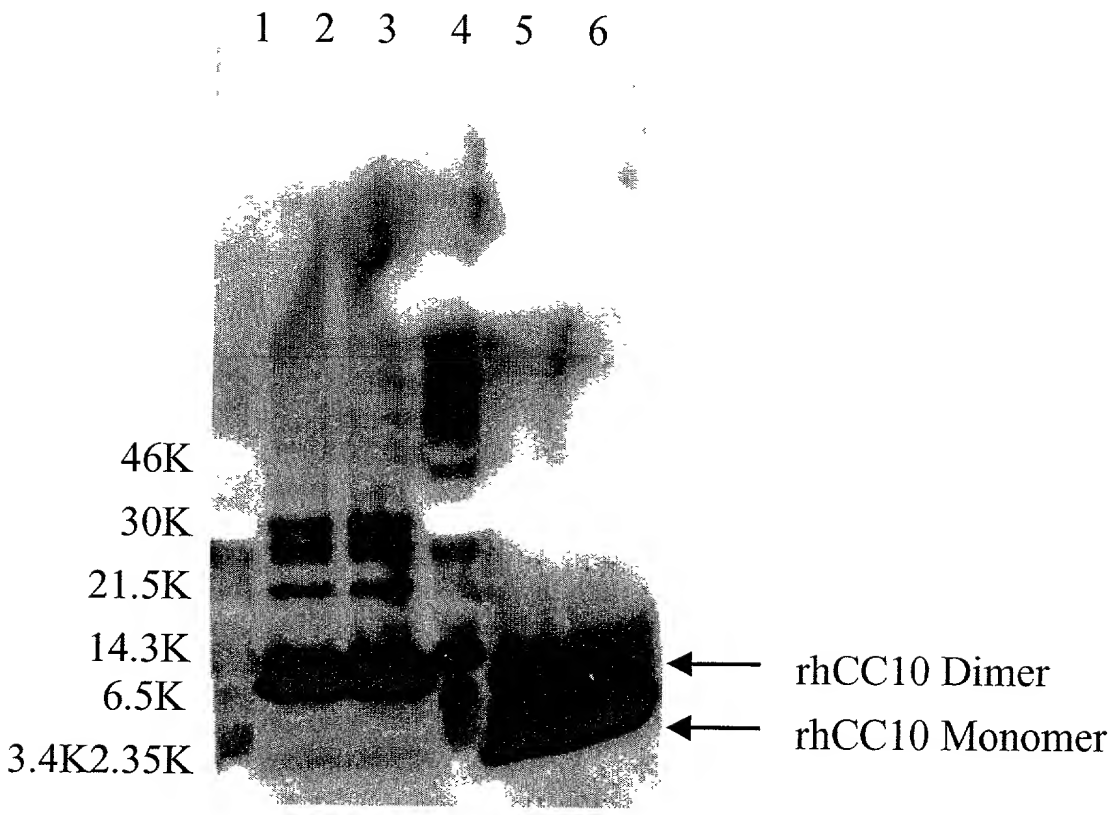

Fig. 28

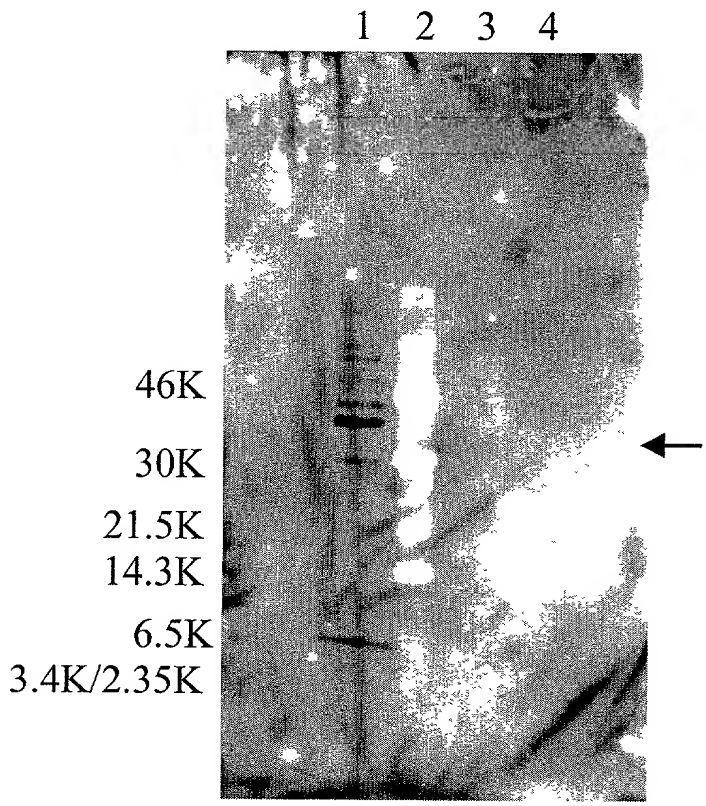

Fig. 29

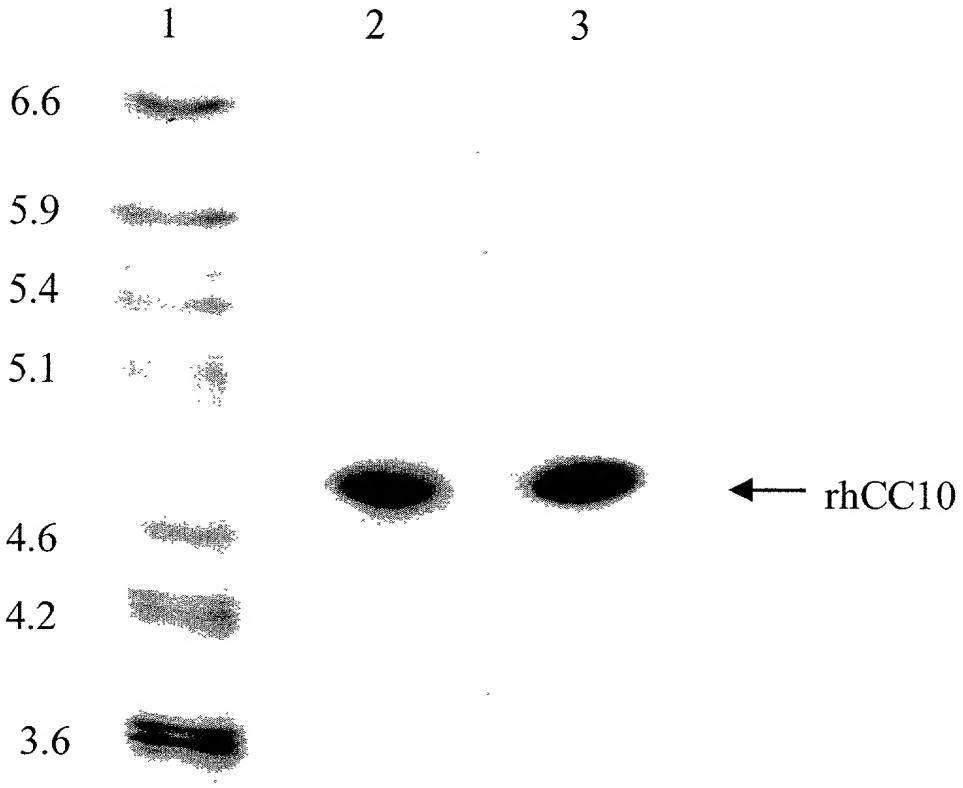

Fig. 30

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CATCGGGATGCCCGCGTTGCAGGCCATGCTGTCCAGGCAGGTAGATGACGACCATCAGGGACAGCTTCAAGGATCGCTCGCGGCTCTTACCAGCCTA
ACTTCGATCATTGGACCGCTGATCGTCACGGCGATTTATGCCGCCTCGGCGAGCACATGGAACGGGTTGGCATGGATTGTAGGCGCCGCCCTATACCT
TGTCTGCCTCCCCGCGTTGCGTCGCGGTGCATGGAGCCGGGCCACCTCGACCTGAATGGAAGCCGGCGGCACCTCGCTAACGGATTCACCACTCCAA
GAATTGGAGCCAATCAATTCTTGCGGAGAACTGTGAATGCGCAAACCAACCCTTGGCAGAACATATCCATCGCGTCCGCCATCTCCAGCAGCCGCAC
GCGGCGCATCTCGGGCAGCGTTGGGTCCTGGCCACGGGTGCGCATGATCGTGCTCCTGTCGTTGAGGACCCGGCTAGGCTGGCGGGGTTGCCTTACTG
GTTAGCAGAATGAATCACCGATACGCGAGCGAACGTGAAGCGACTGCTGCTGCAAAACGTCTGCGACCTGAGCAACAACATGAATGGTCTTCGGTTT
CCGTGTTTCGTAAAGTCTGGAAACGCGGAAGTCAGCGCCCTGCACCATTATGTTCCGGATCTGCATCGCAGGATGCTGCTGGCTACCCTGTGGAACAC
CTACATCTGTATTAACGAAGCGCTGGCATTGACCCTGAGTGATTTTTCTCTGGTCCCGCCGCATCCATACCGCCAGTTGTTTACCCTCACAACGTTCCA
GTAACCGGGCATGTTCATCATCAGTAACCCGTATCGTGAGCATCCTCTCTCGTTTCATCGGTATCATTACCCCCATGAACAGAAATCCCCCTTACACGG
AGGCATCAGTGACCAAACAGGAAAAAACCGCCCTTAACATGGCCCGCTTTATCAGAAGCCAGACATTAACGCTTCTGGAGAAACTCAACGAGCTGGA
CGCGGATGAACAGGCAGACATCTGTGAATCGCTTCACGACCACGCTGATGAGCTTTACCGCAGCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAAC
CTCTGACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAGCGGGTGTTGGCG
GGTGTCGGGGCGCAGCCATGACCCAGTCACGTAGCGATAGCGGAGTGTATACTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCAC
CA

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Fig. 31

Met Ala Ala Glu Ile Cys Pro Ser Phe Gln Arg Val Ile Glu Thr Leu Leu Met Asp Thr Pro Ser Ser Tyr Glu Ala Ala Met Glu Leu Phe Ser Pro Asp Gln Asp Met Arg Glu Ala Gly Ala Gln Leu Lys Lys Leu Val Asp Thr Leu Pro Gln Lys Pro Arg Glu Ser Ile Ile Lys Leu Met Glu Lys Ile Ala Gln Ser Ser Leu Cys Asn